

WHAT IS CLAIMED IS:

1. A method for the transfer of a nucleic acid composition to cells, comprising the step of introducing a multifunctional molecular complex into cells, wherein said multifunctional molecular complex comprises:
  - A) a nucleic acid composition; and
  - B) a transfer moiety comprising
    - (i) one or more cationic polyamine components, wherein each cationic polyamine is non-covalently bound to said nucleic acid composition and comprises from three to twelve nitrogen atoms; and
    - (ii) one or more endosome membrane disruption promoting components attached to at least one nitrogen atom of at least one of said polyamine components through an alkyl, carboxamide, carbamate, thiocarbamate, or carbamoyl bridging group, said one or more endosome membrane disruption promoting components independently selected from (a) at least one lipophilic long chain alkyl group or (b) a fusogenic peptide, cholic acid or cholesteryl group or a derivative thereof;

wherein said multifunctional molecular complex transfers said nucleic acid composition to said cells.
2. A method according to Claim 1 wherein said nucleic acid composition is a nucleic acid molecule that comprises a nucleotide sequence that encodes a peptide or protein, or serves as a template for a nucleic acid molecule.
3. A method according to Claim 2 wherein the peptide, protein or nucleic acid molecule is a product of industrial, commercial or scientific value, selected from the group consisting of therapeutic agents; vaccines; foodstuffs and nutritional supplements; compounds of agricultural significance; herbicides and plant growth regulants; insecticides; miticides; rodenticides; and fungicides; compounds useful in animal health; parasiticides; nematocides.

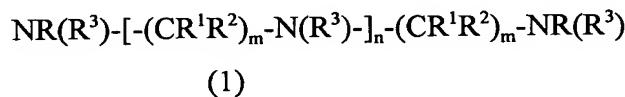
4. A method according to Claim 1 wherein the target cells are cultures of host cells comprising microorganism cells of bacteria, yeast, plant or mammalian cells; said cell cultures being maintained in accordance with fermentation techniques which maximize production of the peptide, protein or functional nucleic acid molecule being produced.

5. A method according to Claim 1 wherein the nucleic acid composition comprises a nucleotide sequence that encodes a protein and is operably linked to regulatory sequences.

6. A method according to Claim 1 wherein the nucleic acid composition comprises a nucleotide sequence that encodes a protein which comprises at least one epitope that is identical or substantially similar to an epitope of an antigen against which an immune response is desired, said nucleotide sequence being operably linked to regulatory sequences.

7. The method according to claim 1, wherein the transfer moiety of said multifunctional molecular complex further comprises at least one receptor specific binding component which is a ligand for a receptor on a target cell.

8. The method according to claim 1, wherein the cationic polyamine comprises the formula (1):



wherein:

$\text{R}$ ,  $\text{R}^1$  and  $\text{R}^2$  are each independently selected from the group consisting of hydrogen and  $\text{C}_{1-6}$  alkyl;

$m$  in each occurrence is independently selected from the integers 2 through 5 inclusive;

n is selected from the integers 1 through 10 inclusive; and R<sup>3</sup> is independently selected from the group consisting of hydrogen; C<sub>1-6</sub> alkyl, an endosome membrane disruption promoting component, and a receptor specific binding component, or NR(R<sup>3</sup>) is guanidino,  
wherein said transfer moiety comprises at least one endosome membrane disruption promoting component attached to at least one nitrogen atom of at least one of said cationic polyamine components.

9. The method according to claim 1, wherein the nucleic acid composition is a plasmid.

10. A method of immunization against a pathogen comprising the step of introducing a multifunctional molecular complex;

wherein said multifunctional molecular complex comprises:

- A) a nucleic acid composition; and
- B) a transfer moiety comprising

(i) one or more cationic polyamine components, wherein each cationic polyamine is non-covalently bound to said nucleic acid composition and comprises from three to twelve nitrogen atoms; and

(ii) one or more endosome membrane disruption promoting components attached to at least one nitrogen atom of at least one of said polyamine components through an alkyl, carboxamide, carbamate, thiocarbamate, or carbamoyl bridging group, said one or more endosome membrane disruption promoting components independently selected from (a) at least one lipophilic long chain alkyl group or (b) a fusogenic peptide, cholic acid or cholesteryl group or a derivative thereof;

wherein said multifunctional molecular complex transfers said nucleic acid composition to said cells,

wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a peptide which comprises at least an epitope identical to, or substantially similar to an epitope displayed on said pathogen as antigen; and wherein said nucleotide sequence is operatively linked to regulatory sequences; and wherein said nucleic acid molecule is capable of being expressed in the cells.

11. A method according to Claim 10 wherein said nucleic acid molecule is a DNA molecule.

12. A method according to Claim 10 wherein said protein is a pathogen antigen or a fragment thereof.

13. A method according to Claim 10 wherein said nucleic acid molecule is administered intramuscularly.

14. A method according to Claim 10 wherein said pathogen is a virus selected from the group consisting of: human immunodeficiency virus, HIV; human T cell leukemia virus, HTLV; influenza virus; hepatitis A virus, HAV; hepatitis B virus, HBV; hepatitis C virus, HCV; human papilloma virus, HPV; Herpes simplex 1 virus, HSV1; Herpes simplex 2 virus, HSV2; Cytomegalovirus, CMV; Epstein-Barr virus, EBV; rhinovirus; and, coronavirus.

15. A method according to Claim 10 wherein at least two or more different nucleic acid molecules are administered to different cells of said individual.

16. A method according to Claim 15 wherein said different nucleic acid molecules each comprise nucleotide sequences encoding one or more pathogen antigens of the same pathogen.

17. The method according to claim 7, wherein the receptor specific binding component is attached through a bridging group to either (i) to a further nitrogen atom of at least one of said cationic polyamine components to which said one or more endosome membrane disruption promoting components is attached, or (ii) to a nitrogen atom of at least one further polyamine component which does not have attached thereto any endosome membrane disruption promoting component.

18. The method according to claim 17, wherein the bridging group through which the receptor specific binding component is attached is selected from the group consisting of an alkyl, carboxamide, carbamate, thiocarbamate, and carbamoyl bridging group.

19. The method according to claim 8, wherein said one or more endosome membrane disruption promoting components are independently selected from the group consisting of:

(a)  $-B-(CR^1R^2)_j-C(R)_3$ , where R is independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl, or C(R)<sub>3</sub> is C<sub>6</sub>H<sub>5</sub> aromatic or absent; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of hydrogen and C<sub>1-6</sub> alkyl; j is an integer from 0 to 24 inclusive; and B is optionally absent, or is a bridging group of the formula:

- (i)  $-(CR^1R^2)_k-C(=O)-Z-$ ;
- (ii)  $-(CR^1R^2)_k-N(R)-C(=O)-Z-$ ;
- (iii)  $-(CR^1R^2)_k-N(R)-\{-C(=O)-CH_2-O-[-(CH_2)_2-O-]_1-(CH_2)_k-N(R)\}_p-C(=O)-Z-$ ; or
- (iv)  $-(CR^1R^2)_k-C(=O)-\{-N(R)-[-(CH_2)_2-O-]_1-CH_2-C(=O)\}_p-Z-$ ;

where k is, independently, an integer from 1 to 11 inclusive, 1 is an integer from 0 to 30 inclusive, and p is an integer from 1 to 3 inclusive; R is independently defined as above or is absent, R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of hydrogen and C<sub>1-6</sub> alkyl; and Z is O, OH, S, N(R), or is absent;

(b)  $-B-(R^4)R$ , where R, R<sup>1</sup> and R<sup>2</sup> are each independently defined as above; B cannot be absent and is a bridging group independently selected from groups (i) through (iv) above, and additionally from the group of the formula:

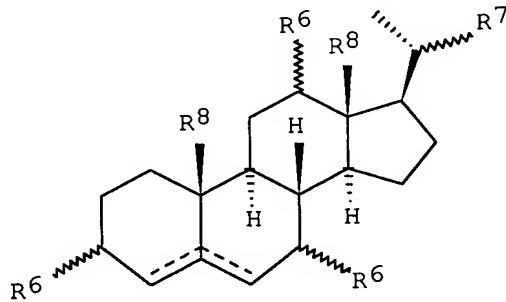
(v)  $-(CR^1R^2)_j-X-$ , where j' is an integer from 1 to 8 inclusive; R<sup>1</sup> and R<sup>2</sup> are each independently defined as above;

X is O, S, N(R), or absent; and

R<sup>4</sup> is independently selected from the group consisting of:

(i) fusogenic peptides comprising spike glycoproteins of enveloped animal viruses;

(ii) cholic acid derivatives of the formula (2):



(2)

where:

www represents a bond of unspecified stereochemistry;

--- represents a single or double bond, forming a

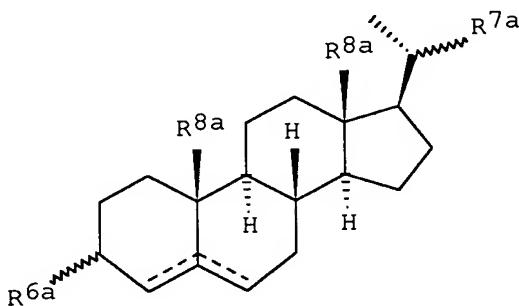
saturated or unsaturated portion of the ring system, provided that they cannot both be unsaturated at the same time, whereby the ring system must be either  $\Delta 4$  or  $\Delta 5$ ;

R<sup>6</sup> is -H, -OH, -CO<sub>2</sub>H, -C(=O)NH<sub>2</sub>, -OC(=O)NH<sub>2</sub>, -NH<sub>2</sub>, or -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>H, where n' is an integer from 1 to 6 inclusive;

R<sup>7</sup> is a radical that forms the point of attachment of the cholic acid derivative, comprising -C<sub>1-6</sub> alkyl- or -C<sub>1-6</sub> alkylcarbonyl-; and

R<sup>8</sup> is C<sub>1-6</sub> alkyl; and

(iii) cholesteryl derivatives of the formula (3):



(3)

where:

www represents a bond of unspecified stereochemistry;

--- represents a single or double bond, forming a

saturated or unsaturated portion of the ring system, provided that they cannot both be unsaturated at the same time, whereby the ring system must be either Δ<sub>4</sub> or Δ<sub>5</sub>;

R<sup>6a</sup> is a radical that forms the point of attachment of the cholesteryl derivative, comprising -C<sub>1-6</sub> alkyl-, -OC(=O)-, or -OCH<sub>2</sub>C(=O)-;

R<sup>7a</sup> is C<sub>1-6</sub> alkyl; and

R<sup>8a</sup> is C<sub>1-6</sub> alkyl.

20. The method according to claim 8, wherein R<sup>3</sup> has the formula:

-B-(R<sup>5</sup>)-R, where B cannot be absent and is a bridging group independently selected from groups (i) through (v) inclusive; R is independently defined or absent; and R<sup>5</sup> is a receptor specific binding component independently selected from the group consisting of:

- (i) D-biotin;
- (ii) β-3'-propionyl galactosyl-β1-4- thioglucoside;
- (iii) N<sup>2</sup>, N<sup>6</sup>-bis(β-3'-propionyl galactosyl-β1-4-thioglucoside)lysine;

(iv)  $N^2, N^6$ -bis( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysyl- $N^6$ -( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysine;

(v) 5-methyltetrahydrofolate;

(vi) folic acid;

(vii) folinic acid;

(viii)  $\alpha$ -3'-propionyl thiomannoside;

(ix)  $\alpha$ -3'-propionyl thiomannoside-6-phosphate; and

(x) an antibody which binds specifically to a cell membrane protein.

21. The method according to claim 8, wherein the cationic polyamine has the formula:  $NH_2-(CH_2)_3-N(R^3)-(CH_2)_4-NH_2$ .

22. The method according to claim 21 wherein  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ , wherein  $C(R)_3$  is  $C_6H_5$  aromatic;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 1; and  $B$  is a bridging group of the formula:  $-(CR^1R^2)_k-C(=O)-Z-$ , wherein  $k$  is 5; and  $Z$  is O.

23. The method according to claim 21 wherein  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(R^4)R$ , wherein  $B$  is a bridging group of the formula:  $-(CR^1R^2)_k-C(=O)-Z-$ ;  $R$  is absent,  $R^1$  and  $R^2$  are each hydrogen;  $k$  is 5,  $Z$  is absent; and  $R^4$  is a fusogenic peptide.

24. The method according to claim 21 wherein  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(R^4)R$ , wherein  $B$  is a bridging group of the formula:  $-(CR^1R^2)_j-X-$ ;  $R$  is absent,  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 5,  $X$  is  $N(R)$ ; and  $R^4$  is a cholic acid derivative wherein  $R^6$  is OH,  $R^7$  is  $C_3$  alkylcarbonyl and  $R^8$  is  $C_1$  alkyl.

25. The method according to claim 21 wherein R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(R<sup>5</sup>)R, wherein R is absent and B is a bridging group of the formula: -(CR<sup>1</sup>R<sup>2</sup>)<sub>k</sub>-N(R)-C(=O)-Z- in which R, R<sup>1</sup> and R<sup>2</sup> are each hydrogen; k is 5, Z is absent; and R<sup>5</sup> is α-3'-propionyl thiomannoside.

26. The method according to claim 21 wherein R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(CR<sup>1</sup>R<sup>2</sup>)<sub>j</sub>-C(R)<sub>3</sub>, wherein C(R)<sub>3</sub> is C<sub>6</sub>H<sub>5</sub> aromatic; R<sup>1</sup> and R<sup>2</sup> are each hydrogen; j is 1 and B is a bridging group of the formula: -(CR<sup>1</sup>R<sup>2</sup>)<sub>k</sub>-N(R)-C(=O)-Z-; k is 5, N(R) is NH and Z is O.

27. The method according to claim 8, wherein the cationic polyamine has the formula NH(R<sup>30</sup>)-(CH<sub>2</sub>)<sub>3</sub>-N(R<sup>3</sup>)-(CH<sub>2</sub>)<sub>4</sub>-N(R<sup>3</sup>)-(CH<sub>2</sub>)<sub>3</sub>-NH(R<sup>30</sup>) wherein:

R<sup>30</sup> is hydrogen or NH(R<sup>30</sup>) is guanidino;  
at least one R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(CR<sup>1</sup>R<sup>2</sup>)<sub>j</sub>-C(R)<sub>3</sub>.

28. The method according to claim 27 wherein:  
R<sup>30</sup> is hydrogen; and  
each R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(CR<sup>1</sup>R<sup>2</sup>)<sub>j</sub>-C(R)<sub>3</sub>,  
wherein C(R)<sub>3</sub> is C<sub>6</sub>H<sub>5</sub> aromatic; R<sup>1</sup> and R<sup>2</sup> are each hydrogen; j is 1; and B is a bridging group of the formula: -(CR<sup>1</sup>R<sup>2</sup>)<sub>k</sub>-N(R)-C(=O)-Z-; where k is 5; N(R) is NH; and Z is O.

29. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen; and  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ,  
wherein B is absent, R,  $R^1$  and  $R^2$  are each hydrogen; and j is 7.

30. The method according to claim 27 wherein:  
 $NH(R^{30})$  is guanidino; and  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ,  
wherein B is absent, R,  $R^1$  and  $R^2$  are each hydrogen; and j is 7.

31. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
one  $R^3$  is hydrogen; and  
one  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(R^4)-R$ ,  
wherein R is absent and B is a bridging group of the formula:  
 $-(CR^1R^2)_j-X-$ , in which R,  $R^1$  and  $R^2$  are each hydrogen;  
j' is 5; and X is  $N(R)$  and  
where  $R^4$  is a type (iii) cholestryl derivative of formula (3):  
 $R^{6a}$  is  $O-C(=O)-$  and a point of attachment of cholestryl derivative;  
 $R^{7a}$  is  $C_5$  alkyl; and  
 $R^{8a}$  is  $C_1$  alkyl.

32. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ,  
wherein B is a bridging group of the formula:  
 $-(CR^1R^2)_k-C(=O)-Z-$ ;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 0,  $k$  is 11; Z is  $N(R)$  where R is  $C_1$  alkyl and  $C(R)_3$  is  $CH_3$ .

33. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ;  
wherein B is a bridging group of the formula:  $-(CR^1R^2)_k-C(=O)-Z-$ ;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 1,  $k$  is 11; Z is O and  $C(R)_3$  is  $C_6H_5$  aromatic.

34. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ;  
wherein B is a bridging group of the formula:  $-(CR^1R^2)_k-C(=O)-Z-$ ;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 0,  $k$  is 11; Z is OH and  $C(R)_3$  is absent.

35. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
one  $R^3$  is hydrogen; and  
one  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ;

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wherein B is a bridging group of the formula:  $-(CR^1R^2)_k-$   
 $C(=O)-Z-$ ;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 1,  $k$  is 11; Z is O and  $C(R)_3$  is  $C_6H_5$  aromatic.

36. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
one  $R^3$  is hydrogen; and  
one  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ ;  
wherein B is a bridging group of the formula:  $-(CR^1R^2)_k-$   
 $C(=O)-Z-$ ;  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 0,  $k$  is 11; Z is OH and  $C(R)_3$  is absent.
37. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
each  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(R^5)R$ ;  
wherein R is absent and B is a bridging group of the formula:  $-(CR^1R^2)_k-N(R)-C(=O)-Z-$ , in which R,  $R^1$  and  $R^2$  are each hydrogen; k is 5; Z is absent and  
 $R^5$  is  $\alpha$ -3'-propionyl thiomannoside.
38. The method according to claim 27 wherein:  
 $R^{30}$  is hydrogen;  
one  $R^3$  is hydrogen; and  
one  $R^3$  is an endosome membrane disruption promoting component of the formula  $-B-(R^5)R$ ;

wherein R is absent and B is a bridging group of the formula:

$-(CR^1R^2)_k-N(R)-\{-(C=O)-CH_2-O-[-(CH_2)_2-O-]_1-(CH_2)_k-N(R)\}_p-C(=O)-Z-$  in which R, R<sup>1</sup> and R<sup>2</sup> are each hydrogen; k is 5; l is 5; p is 1; Z is absent; and

R<sup>5</sup> is  $\alpha$ -3'-propionyl thiomannoside.

39. The method according to claim 27 wherein:

R<sup>30</sup> is hydrogen;

one R<sup>3</sup> is hydrogen; and

one R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(R<sup>5</sup>)R;

wherein R is absent and B is a bridging group of the formula:

$-(CR^1R^2)_k-N(R)-\{-(C=O)-CH_2-O-[-(CH_2)_2-O-]_1-(CH_2)_k-N(R)\}_p-C(=O)-Z-$  in which R, R<sup>1</sup> and R<sup>2</sup> are each hydrogen; k is 5; l is 20; p is 1; Z is absent; and

R<sup>5</sup> is  $\alpha$ -3'-propionyl thiomannoside.

40. The method according to claim 27 wherein:

R<sup>30</sup> is hydrogen;

one R<sup>3</sup> is hydrogen; and

one R<sup>3</sup> is an endosome membrane disruption promoting component of the formula -B-(R<sup>5</sup>)R;

wherein R is absent and B is a bridging group of the formula:

$-(CR^1R^2)_k-N(R)-\{-(C=O)-CH_2-O-[-(CH_2)_2-O-]_1-(CH_2)_k-N(R)\}_p-C(=O)-Z-$  in which R, R<sup>1</sup> and R<sup>2</sup> are each hydrogen; k is 5; l is 5; p is 1; Z is absent; and

R<sup>5</sup> is N<sup>2</sup>, N<sup>6</sup>-bis( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysyl-N<sup>6</sup>-( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysine.

41. The method according to claim 8, wherein said transfer moiety comprises more than one cationic polyamine component.

42. The method according to claim 8, wherein a first cationic polyamine component comprises an endosome membrane disruption promoting component and a second cationic polyamine component comprises a receptor specific binding component.

43. The method according to claim 42, wherein the first cationic polyamine component has an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ , wherein  $C(R)_3$  is absent,  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 0 and  $B$  is a bridging group selected from the group consisting of (i), (ii), (iii) and (iv).

44. The method according to claim 42, wherein the first cationic polyamine component has an endosome membrane disruption promoting component of the formula  $-B-(CR^1R^2)_j-C(R)_3$ , wherein  $C(R)_3$  is absent,  $R^1$  and  $R^2$  are each hydrogen;  $j$  is 0 and  $B$  is a bridging group of the formula:  $-(CR^1R^2)_k-C(=O)-Z-$ ;  $k$  is 11 and  $Z$  is OH.

45. The method according to claim 42, wherein the first cationic polyamine component has an endosome membrane disruption promoting component of the formula  $-B-(R^4)R$ , wherein  $R^4$  is a cholesteryl derivative.

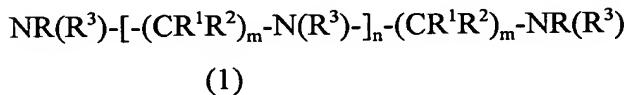
46. The method according to claim 42, wherein the first cationic polyamine component has an endosome membrane disruption promoting component of the formula  $-B-(R^4)R$ , wherein  $R$  is absent and  $B$  is a bridging group of the formula:  $-(CR^1R^2)_{j'}-X-$ , in which  $R$ ,  $R^1$  and  $R^2$  are each hydrogen;  $j'$  is 5; and  $X$  is  $N(R)$  and where  $R^4$  is a type (iii) cholesteryl derivative of formula (3):  $R^{6a}$  is  $O-C(=O)-$  and a point of attachment of cholesteryl derivative;  $R^{7a}$  is  $C_5$  alkyl; and  $R^{8a}$  is  $C_1$  alkyl.

47. The method according to claim 42, wherein the receptor specific binding component of said second cationic polyamine component is selected from the group consisting of:

$\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside;  
 $N^2, N^6$ -bis( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysine;  
 $N^2, N^6$ -bis( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysyl- $N^6$ -( $\beta$ -3'-propionyl galactosyl- $\beta$ 1-4-thioglucoside)lysine;  
 $\alpha$ -3'-propionyl thiomannoside; and  
 $\alpha$ -3'-propionyl thiomannoside-6-phosphate.

48. A method for delivering a nucleic acid molecule to a targeted population of cells of an individual, said method comprising the step of delivering to the individual a multifunctional molecular complex comprising:

- A) a nucleic acid molecule; and
- B) a transfer moiety comprising one or more cationic polyamine components, wherein each cationic polyamine is non-covalently bound to said nucleic acid molecule and each independently comprises a cationic polyamine of the formula (1):



wherein:

$R, R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen and  $C_{1-6}$  alkyl;

$m$  in each occurrence is independently selected from the integers 2 through 5 inclusive;

$n$  is selected from the integers 1 through 10 inclusive;

$R^3$  is independently selected from the group consisting of hydrogen; C<sub>1-6</sub> alkyl, and an endosome membrane disruption promoting component, or NR( $R^3$ ) is guanidino;

wherein said transfer moiety comprises at least one endosome membrane disruption promoting component attached to at least one nitrogen atom of at least one of said cationic polyamine components;

wherein said transfer moiety comprises at least one receptor specific binding component attached either (i) to a further nitrogen atom of at least one of said cationic polyamine components to which said one or more endosome membrane disruption promoting components is attached, or (ii) to a nitrogen atom of at least one further polyamine component which does not have attached thereto any endosome membrane disruption promoting component,

wherein said receptor specific binding component which is a ligand for natural receptors of said target cells.